APPENDIX A

PRELIMINARY RISK ASSESSMENT

State of California

Memorandum

To : Jim Wells
Director

Date : February 11, 1992

Place : Sacramento

4-1285

From : Department of Pesticide Regulation - Larry Nelson, Chief
Medical Toxicology Branch

Subject : Methyl Bromide Preliminary Risk Characterization

We have completed a preliminary risk characterization of methyl bromide to evaluate the significance of ambient air levels resulting from structural fumigation and agricultural uses. Attached are evaluations, conducted by the Branch, which provide the specifics of our analysis.

Results indicate inadequate margins of safety exist from methyl bromide exposure for both existing uses.

Attachment

SURNAME

State of California

Memorandum

To : Larry Nelson, Chief

Date : February 11, 1992

Place : Sacramento, CA

via Keith Pfeifer, Senior Toxicologist

From : **Department of Pesticide Regulation** Lori O. Lim
Staff Toxicologist

Subject : Methyl Bromide- Preliminary risk assessment for inhalation exposure in structural fumigation

INTRODUCTION

Methyl bromide is used in structural, soil, and commodity fumigation. In 1991, more than 60 products as technical material or formulations were registered in California. The major registrants are Ameribrom, TriCal, Soil Chemical Corp., Ethyl Corp., and Great Lakes Chemical Corp. The use of methyl bromide has been increasing in the last 5 years. The amount applied doubled from 10 million pounds in 1986 to over 20 million pounds in 1991.

The current label for the use of methyl bromide in domestic dwellings specifies re-entry at an air concentration below 5 ppm. However, there were two Section 24 (c) SLN issued in 1990 for scale broom roots in buildings (CA-900038 and CA-900045) where the re-entry level should not exceed 30 ppb. This level was recommended by Worker Health & Safety Branch based on the NOEL of 3 ppm from the rat reproductive study to achieve a Margin of Safety (MOS) of 100.

Since its use commercially, worker illnesses have been reported as early as 1899 (von Oettingen, 1946). Dermal exposure to high concentrations of methyl bromide results in vesication and swelling of the skin (Butler, *et al.*, 1945 and Jordi, 1953). Signs and symptoms of methyl bromide from inhalation exposure are dependent on the amount and duration of exposure (Greenberg, 1971; Gehring, *et al.*, 1991). Mild and chronic exposure results in polyneuropathy which may be reversible. Acute exposure to high concentrations results in: malaise, headache, visual disturbances, nausea, and vomiting. There is a delayed onset of symptoms indicative of central nervous system involvement: numbness, ataxia, tremor, convulsion, and coma. Death is usually due to pulmonary edema leading to respiratory failure or cardiovascular collapse.

In a study of workers in a repackaging plant where the methyl bromide was estimated to be less than 35 ppm (or approximately 12 mg/kg-day), clinical symptoms of anorexia, nausea, headache, vertigo, abnormal sleepiness were reported (Watrous, 1942).

ACUTE EXPOSURE

In animal studies, acute exposure to methyl bromide resulted in central nervous system depression and loss of righting reflex (Honma, *et al.*, 1985) and decreased body weight gain (Honma, *et al.*, 1985; Alexeeff and Kilgore, 1985). At higher concentrations, there were decrease in body temperature, lethargy (Honma, *et al.*, 1985; Alexeeff and Kilgore, 1985), excitability (Irish, *et al.*, 1940), and paralysis (Irish, *et al.*, 1940). The alteration in body temperature, anorexia resulting in lower body weight gain, and inactivity has been attributed to methyl bromide inhibition of tyrosine hydroxylase activity (Honma, *et al.*, 1991). Developmental toxicity studies indicate that methyl bromide is a developmental toxin in the rat and rabbit (Breslin, *et al.*, 1990; Sikov, *et al.*, 1981).

SURNAME Lim | D.F. Lim

The lowest acute NOEL was 40 ppm (155 mg/m^3) from the rabbit teratology study (Breslin, *et al.*, 1990). The endpoints (80 ppm, or 310 mg/m^3) (in the fetus) were omphalocele, hemorrhaging with or without hydrops, retroesophageal right subclavian artery, gall bladder agenesis, fused sternebrae and decreased fetal body weights. The duration adjusted dosage (amortized over 24 hrs exposure, 7 days per week, and respiration rate of ~~960~~ 540 L/kg/day) for the NOEL is 21 mg/kg-day.

Based on the NOEL of 21 mg/kg-day and the exposure at the re-entry level of 5 ppm, the margin of safety for human exposure is 4 and is inadequate. Generally, when animal data is used, an MOS of 100 is considered adequate. Although teratogenic endpoints are only relevant for women of child-bearing age, the assumption that all other population subgroups are as sensitive results in MOSs that protect the health of other population subgroups.

Subgroup	Breathing rate m^3/kg-day	Human equivalent NOEL (ppm)	MOS
Adult	0.26	21	4

SUBCHRONIC EXPOSURE

After structural fumigation, the residents of the houses can potentially be exposed to methyl bromide for a short term as it is released from the structure and furnishings.

In animal studies, inhalation exposure to methyl bromide subchronically resulted in tissue degeneration (Hurtt, *et al.*, 1987), lung lesions (Irish, *et al.*, 1940), decreased body and organ weights (American Biogenics Corp., 1986), reduced fertility (American Biogenics Corp., 1986), fetal variations (Sikov, *et al.*, 1981; Breslin, *et al.*, 1990), and neurotoxicity and convulsions (Irish, *et al.*, 1940; Breslin, *et al.*, 1990; Sikov, *et al.*, 1981; NTP, 1990).

The lowest NOEL was 20 ppm (78 mg/m^3, adjusted dosage of 12 mg/kg-day) for neurotoxicity (convulsion, paresis, and death) observed in rabbits exposed to methyl bromide for more than 1 week (Sikov, *et al.*, 1981). Neurotoxicity after methyl bromide exposure has also been reported in the monkey (NOEL of 13 mg/kg-day), mouse (NOEL of 31 mg/kg-day), and in another rabbit study (NOEL of 21 mg/kg-day).

The reproductive study used previously in the SLN application is not used in this assessment because the effects were not observed until after more than 100 days of treatment. The re-entry level is evaluated based on a shorter duration of exposure for normal fumigation as compared to subfloor methyl bromide injection which demonstrated air levels > 30 ppb for up to 21 days post treatment.

Based on the NOEL of 12 mg/kg-day and the exposure at the re-entry level of 5 ppm, the margins of safety for human exposure are inadequate. Again, an MOS of 100 is generally considered adequate.

Subgroups	Breathing rate m^3/kg-day	Human equivalent NOEL (ppm)	MOS
Adult	0.26	12	2
Child	0.46	7	1

RECOMMENDATION

As indicated in this preliminary assessment, the current re-entry level of 5 ppm does not provide adequate margins of safety. Based on the subchronic exposure of children, the highest potential exposure population subgroup, an air concentration not to exceed 60 ppb in 24 hours is needed to provide an MOS of 100.

State of California

Memorandum

To : Larry Nelson, Chief
Medical Toxicology Branch

Date : February 11, 1992

Place : Sacramento

via Keith Pfeifer, Senior Toxicologist
Health Assessment Section

From : Department of Pesticide Regulation
Nu-may R. Reed
Staff Toxicologist

Subject : Acute exposures to airborne Methyl Bromide

The potential health effects of airborne methyl bromide was re-evaluated.

Background Information

A report documenting air monitoring data by the Air Resources Board (ARB) under the mandate of AB1807 was received by Medical Toxicology Branch in November, 1990. Using these data, a preliminary risk assessment was initially conducted in December, 1990. Based on the toxicological data available at the time, an interim NOEL of 90 ppm (6 hr/day; 5 days) established in a rat subchronic study (DPR Vol.123-109) was used in the assessment. The margin of safety (MOS) ranged from 104 (child) to 185 (adult). The toxicological database has since been updated.

In a recent evaluation of the potential health hazards associated with the label-approved use for structural fumigation, the staff established an inhalation NOEL to evaluate acute exposure scenarios. Consequently, the potential health hazard associated with the occurrence of methyl bromide in the air was re-assessed.

Air monitoring data

The air monitoring for field application was conducted in Monterey county, at town sites and sites adjacent to the application field (off-site). Air samples were also taken after enclosure fumigation in Stockton. The results are given in the attached Summary table from the ARB report.

Based on this report, the air concentrations of 1.1 ppb (Minimum Detection Limit, MDL) and 450 ppb were used for assessing the exposures for town sites and off-sites, respectively. The 450 ppb was the average air concentration for an approximately 24-hour period (Sept. 12, 9:45 am to Sept. 13, 1:15 pm), based on three 3-hour measurements for site B at Fennell farm (67 meter from the edge of an application site). A summary table (ARB report, Table 8) of the air measurements at this site is also attached. The highest single measurement at the Stockton sites was 1.6 ppb.

Toxicological data

The acute inhalation NOEL was established at 21 ppm for women of child-bearing age. These values were calculated from the NOEL of 21 mg/kg/day (40 ppm; 6 hr/day), for developmental effects established in a rabbit teratology study. Using this NOEL to evaluate the risk of women of child-bearing age will provide the lowest MOS among all population subgroups. The supporting

SURNAME

toxicological database is presented in greater detail in the memo from Lori Lim to Larry Nelson (February 11, 1992) concerning structural fumigation.

Risk Characterization

Based on the human NOEL of 21 ppm and the ARB monitoring data, the margins of safety (MOSs) for the Monterey county town sites (air concentration at the MDL of 1.1 ppb) and sites at Stockton (highest concentration at 1.6 ppb) are at least 13,000 and indicate no potential health concern. The MOS for the acute off-site exposures at 450 ppb is 47. An MOS of 100, based on a NOEL established in animal studies, is generally considered adequate. The off-site air measurement, taken 67 meters from the edge of an application site, represents a realistic exposure scenario, since no buffer zone is currently required for methyl bromide field application.

Recommendation

Reduction of the air levels to an equivalence of 210 ppb for 24 hours would result in an MOS of 100, which is generally considered adequate based on a NOEL established in animal studies.

Attachment

Attachment: Summary tables of ARB's air monitoring report

Summary Table

Summary of Air Concentrations of Methyl Bromide in Parts Per Billion Volume

(4-hour samples collected in September and October 1986)

Monitoring Site	Maximum Positive[a]	Second Highest Positive[a]	Average All Samples above MDL	Total # of Samples	# Above MDL[b]
Aromas	~MDL	~MDL	<MDL	48	2
Elkhorn	<MDL	<MDL	<MDL	46	0
Flea Market	<MDL	<MDL	<MDL	48	0
M. P. Hospital	<MDL	<MDL	<MDL	42	0
Fennell Farms[c]					
Site A	210	52	76.8	22	8
Site B	900	280	111	38	25
Site C	530	110	59.4	36	20
Stockton	1.6	0.92	1.0	87	3

[a]Average of two replicates, rounded to two significant figures.

[b]MDL = minimum detection limit (1.1 ppb; 0.5 ppb for Stockton samples).

[c]Sites A-C were adjacent to a strawberry field application.

Table 8. METHYL BROMIDE AT FENNELL FARMS APPLICATION SITE
(average values)

DATE	START TIME	(µg/Cu m) SITE A	SITE B	SITE C	(P.P.B.) SITE A	SITE B	SITE C
9/11/86							
	7:10		197			51	
	8:54	200			52		
	11:25		284			73	
	11:37			422			110
	13:30	< 4.2			< 1.1		
9/12/86							
	6:20		< 4.2			< 1.1	
	6:23			< 4.2			< 1.1
	7:00	800			210		
	9:45		1100			280	
	10:15			325			84
	10:57	< 4.2			< 1.1		
	13:02		3500			900	
	13:30			2060			530
9/13/86							
	10:15		668			170	
	10:45			400			100
	13:45		409			110	
	14:18			273			70
9/14/86							
	8:45		89			23	
	8:50			29			7.0
	9:18	< 4.2			< 1.1		
	12:50		621			160	
	13:30			212			55
9/15/86							
	7:00		< 4.2			< 1.1	
	7:25			< 4.2			< 1.1
	7:55	157			41		
	11:18		230			59	
	11:38			62			16
	11:59	< 4.2			< 1.1		
	15:25		315			81	
	15:45			215			55
	19:46		449			116	
	20:02			162			42
9/16/86							
	7:22		< 4.2			< 1.1	
	7:52			< 4.2			< 1.1
	8:16	17			4.0		
	11:19		< 4.2			< 1.1	
	12:29			< 4.2			< 1.1
	12:55	< 4.2			< 1.1		
	17:05		50			13	
	17:26			< 4.2			< 1.1
9/17/86							

Table 8 (con't). METHYL BROMIDE AT FERRELL FARMS APPLICATION SITE

(average values)

DATE	START TIME	(µg/Cu m) SITE A	SITE B	SITE C	(P.P.B.) SITE A	SITE B	SITE C
	9:47			< 4.2			< 1.1
	10:11		< 4.2			< 1.1	
	10:36	< 4.2			< 1.1		
	14:18			< 4.2			< 1.1
	15:22		38			10	
9/18/86							
	8:56	< 4.2			< 1.1		
	9:33		< 4.2			< 1.1	
	9:59			< 4.2			< 1.1